

# Etiology and prevalence of hyponatremia in geriatric patients with fragility hip fractures

Hyponatremia in geriatric patients with fragility hip fractures

Emine Emektar, Seda Dagar, Hüseyin Uzunosmanoğlu, Fatmanur Karaaslan, Şeref Kerem Çorbacıoğlu, Yunsur Çevik  
Department of Emergency Medicine, Keçiören Training and Research Hospital, Ankara, Turkey

## Abstract

**Aim:** In this study, we aimed to determine the prevalence and etiological factors of hyponatremia among geriatric patients, who presented to the emergency department (ED) with simple mechanical falls and were diagnosed with a hip fragility fracture, and to compare these patients' clinical course with that of patients with a normal serum sodium level.

**Material and Method:** This study is a retrospective study. Patients aged 65 years or older, admitted to the ED with hip fragility fracture, were enrolled in the study. The patients' serum sodium level at admission was evaluated. Study data were analyzed with IBM SPSS 20.0 (Chicago, IL, USA) /statistical software.

**Results:** This study enrolled 646 patients; 30.5 % of the patients were male and the median age was 85 (IQR 25-75, 78-89) years. Hyponatremia was present in 16.4% (n=106) of the patients.

A comparison of the normonatremic and hyponatremic patients showed that the hyponatremic ones had a greater prevalence of osteoporosis, proton pump inhibitor (PPI), and diuretic use, a higher creatinine level, and a lower hematocrit level ( $p=0.002$ ,  $p=0.042$ ,  $p=0.008$ ,  $p=0.023$ ,  $p=0.001$ , respectively).

**Discussion:** Hip fractures are emergency conditions associated with high mortality, which are especially common in the elderly. We showed a considerable prevalence of hyponatremia in geriatric hip fractures. We believe that mild chronic hyponatremia is one of the important risk factors for fragility hip fracture. The majority of hyponatremia cases are the result of comorbidities and polypharmacy.

## Keywords

Fragility fracture; Hyponatremia; Geriatric

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Corresponding Author: Emine Emektar, Department of Emergency Medicine, Keçiören Training and Research Hospital, Pınarbaşı, Sanatoryum Street No:25, 06280, Keçiören, Ankara, Turkey.

E-mail: emineakinci@yahoo.com P: +90 5055562675

Corresponding Author ORCID ID: <https://orcid.org/0000-0002-6056-4401>

## Introduction

Hip fractures are particularly common in the geriatric age group. They represent injuries with potentially increased morbidity and mortality rates due to certain factors related to the elderly population, such as limited physiological reserve, preoperative medical conditions, and a combination of trauma and major surgery [1, 2]. The mean survival of elderly people treated for hip fractures is shorter than that of the same age group without hip fractures [3].

A fragility fracture is a fracture resulting from a fall from standing height or less. These fractures, which most commonly occur in the hip, spine, or wrist, are an indication that the bones of the body have been weakened by underlying conditions [4, 5]. The risk factors for hip fragility fractures are advanced age, sex, race, weight loss, lack of exercise, nutritional disorders, metabolic disorders, smoking, and alcohol use. The majority of fractures of the femur neck are associated with osteoporosis-induced loss of bone mass [4]. Less commonly, other metabolic disorders such as osteomalacia and renal osteodystrophy, oncological diseases, and endocrinological disorders like diabetes mellitus (DM) and hyperthyroidism are also related to hip fractures. In addition to changes in bone mass, falls secondary to muscle strength and coordination problems, as well as inadequate absorption of fall energy play role in developing fall-associated fractures in the elderly [5]. Additionally, hyponatremia and hyponatremia-induced imbalance may be exemplified as metabolic disorders predisposing to falls [6, 7]. Plasma sodium concentration is the main determinant of plasma osmolality. Maintaining plasma sodium concentration and plasma osmolality at relatively constant levels is of paramount importance for maintaining cellular volume, especially in the brain. Alterations in sodium concentration may cause a series of abnormalities ranging from mild neurological signs (imbalance, vertigo, headache, confusion) to seizures, coma, and even death [6]. A review of the literature suggests that sodium disorders are common in the elderly; hyponatremia, in particular, may cause falls as a result of altered consciousness, such as confusion and delirium or balance problems [7-9].

In our study, we aimed to determine the prevalence and etiological factors of hyponatremia among geriatric patients presenting to the emergency department (ED) with simple mechanical falls who were diagnosed with a hip fragility fracture and to compare their clinical course with that of patients with a normal serum sodium level.

## Material and Methods

### Design and setting

Our retrospective study was conducted in a tertiary care ED with approximately 250,000 patient admissions per year. Prior to its implementation, our study's protocol was approved by the local ethics committee (2012-KAEK-15/2023, 25/12/2019). As this is a retrospective study, the participants' informed consent was not required.

### Study population

This study involved patients admitted to the ED between 01.01.2014-01.11.2019, who were diagnosed with a hip fragility fracture, recorded with ICD codes of S72.00 (femur neck fracture), S72.10 (pertrochanteric fracture) and S72.20

(subtrochanteric fracture).

Fragility hip fracture was defined as any hip fracture that occurred in the absence of trauma or in the presence of a low-energy trauma resulting from a fall from a height equal to or less than 1 m. Patients with hip fractures caused by other mechanisms were excluded. Plasma sodium level that was less than 135 mmol/L was labeled as hyponatremia. The patients were categorized into mild hyponatremia (130-134 mmol/L), moderate hyponatremia (125-129 mmol/L), and severe hyponatremia (<125 mmol / L) groups, based on their serum sodium levels. The demographic information, comorbid disorders (systemic hypertension, diabetes mellitus, pulmonary disease, hypothyroidism, heart failure, ischemic heart disease, osteoporosis, dementia) medication use (selective Serotonin Reuptake Inhibitors (SSRI), Proton pump inhibitors (PPI), diuretics (thiazides and/or loop diuretics), vital signs, results of laboratory and imaging studies taken at admission, and 30-day mortality rate were recorded.

Patients with missing data were excluded.

### Statistical Analysis

Study data were analyzed using IBM SPSS 20.0 (Chicago, IL, USA) statistical software. The normality of discrete and continuous variables was tested using the Kolmogorov-Smirnov test. Descriptive statistics included median and IQR25-75 (interquartile range) for discrete and continuous variables and number and (%) for categorical variables. Categorical variables were compared using the Chi-square test and continuous variables using the Mann-Whitney U test.

The results were considered statistically significant at a level of  $p < 0.05$ .

## Results

Initially, this study enrolled 744 patients. Ninety-eight patients with missing data were excluded, and the remaining 646 were included in the final analysis; 30.5 % of the patients were male and the median age was 85 (IQR 25-75, 78-89) years. The most common comorbidity was hypertension. PPI use was recorded in 57.1% of the patients. The median duration of hospital stay was 6 (IQR 25-75, 4-8) days; the 30-day mortality rate was 10.8% (n=70). The demographic data of the study population are presented in Table 1.

The blood tests performed at ED admission revealed hyponatremia in 16.4% (n=106) of the patients. A comparison of normonatremic and hyponatremic patients showed higher rates of osteoporosis, PPI and diuretic use; a higher creatinine level; and a lower hematocrit level in the hyponatremia group ( $p=0.002$ ,  $p=0.042$ ,  $p=0.008$ ,  $p=0.023$ ,  $p=0.001$ , respectively) (Table 2). There was no significant difference between the two groups with respect to other comorbidities, medications, type of fracture, laboratory results, Time from admission to surgery, duration of hospital stay, and mortality rate (for all parameters  $p > 0.05$ ) (Table 2).

## Discussion

Hip fracture is an emergency condition that is especially common in the geriatric population, and it is associated with increased mortality and morbidity. In the present study, we examined the incidence of hyponatremia among geriatric

**Table 1.** Demographic data of the patients (n=646)

Sex n (%)	Male	197 (30.5%)
	Age, years, median (IQR 25-75)	85 (78-89)
Comorbidity n (%)	Hypertension	429 (66.4%)
	Diabetes Mellitus	166 (25.7%)
	Coronary heart disease	223 (34.5%)
	Chronic heart failure	83 (12.8%)
	Chronic renal failure	81 (12.5%)
	Hypothyroidism	35 (5.4%)
	Dementia	110 (17%)
	COPD	60 (9.3%)
	Osteoporosis	141 (21.8%)
Drugs n (%)	Antidepressant	54 (8.4%)
	PPI	369 (57.1%)
	Diuretic	88 (13.6%)
Type of fracture n (%)	Head	6 (0.9%)
	Neck	217 (33.6%)
	Perthrochanteric	212 (32.8%)
	Subtrochanteric	211 (32.7%)
	Hyponatremia n (%)	106 (16.4%)
Hyponatremia severity n (%)	Mild	92 (86.8%)
	Moderate	8 (7.5%)
	Severe	6 (5.7%)
Laboratory median (IQR 25-75)	Hematocrit	36.1 (32.2-39.7)
	Glucose	133 (113-178)
	Sodium	139 (136-140)
	BUN mg/dL	47 (36.3-62)
	Creatinine mg/dL	0.9 (0.76-1.2)
	Albumin g/dL	3.6 (3.1-3.8)
	Hospital stay duration, (days) median (IQR 25-75)	6 (4-8)
	Time to surgery from admission, (days) median (IQR 25-75)	2 (1-3)
	30-day mortality n (%)	70 (10.8%)

COPD: chronic obstructive pulmonary disease, PPI: proton pump inhibitor, BUN: Blood Urea Nitrogen

patients with fragility hip fracture, and reached two important conclusions.

Firstly, we found that among geriatric patients, who developed hip fracture secondary to simple mechanical falls, the incidence of hyponatremia was 16.4%, and 13.2% of all hyponatremia cases were moderate/severe. The majority of patients who were found to have a reduced sodium level, thus had mild asymptomatic hyponatremia. Secondly, we observed that the prevalence of osteoporosis and PPI and diuretic use were higher among patients with hypernatremia, although we did not demonstrate any significant difference between other parameters. The majority of hyponatremia cases may have resulted from polypharmacy and is associated with inappropriate ADH syndrome.

A fragility fracture is an injury that influences morbidity and mortality rates in the elderly after simple trauma, and it occurs as a result of a number of factors, including hyponatremia [7]. Hyponatremia is one of the most commonly known electrolyte disorders in the elderly [9]. It is usually of mild severity (130-135 mmol/L) and has a chronic course (lasting for >48 hours) [10]. Although its prevalence differs between the older people

**Table 2.** Characteristics of the patients according to sodium levels

Sex	Characteristic	Hyponatremic participants (n=106)	Normonatremic participants (n=540)	P-value
Sex n (%)	Male	30 (28.3%)	167 (30.9%)	0.592
	Age, years, median (IQR 25-75)	83 (76-88)	85 (79-89)	0.082
Comorbidity n (%)	Hypertension	74 (69.8%)	355 (65.7%)	0.417
	Diabetes Mellitus	34 (32.1%)	132 (24.4%)	0.100
	Coronary heart disease	44 (41.5%)	179 (33.1%)	0.098
	Chronic heart failure	14 (13.2%)	69 (12.8%)	0.904
	Chronic renal failure	14 (13.2%)	67 (12.4%)	0.913
	Hypothyroidism	9 (8.5%)	26 (4.8%)	0.126
	Dementia	20 (18.9%)	90 (16.7%)	0.581
	COPD	13 (12.3%)	47 (8.7%)	0.248
	Osteoporosis	35 (33%)	106 (19.6%)	0.002
Drugs n (%)	Antidepressant	9 (8.4%)	45 (8.3%)	0.983
	PPI	70 (66%)	299 (55.4%)	0.042
	Diuretic	23 (21.7%)	65 (12%)	0.008
Type of fracture n (%)	Head	2 (1.9%)	4 (0.7%)	
	Neck	37 (34.9%)	180 (33.3%)	0.611
	Perthrochanteric	33 (31.1%)	179 (33.1%)	
	Subtrochanteric	34 (32.1%)	177 (32.8%)	
Laboratory median (IQR 25-75)	Hematocrit	34.6 (30.9-38.1)	36.5 (32.5-39.8)	0.001
	Glucose	146 (109-203)	133 (113-173)	0.123
	BUN mg/dL	48 (38.3-75.4)	47 (36.3-60)	0.104
	Creatinine mg/dL	0.97 (0.80-1.28)	0.90 (0.75-1.17)	0.023
	Albumin g/dL	3.5 (3.1-3.8)	3.6 (3.1-3.87)	0.584
	Hospital stay duration, (days) median (IQR 25-75)	6 (3.7-8)	6 (4-8)	0.329
	Time to surgery from admission, (days) median (IQR 25-75)	2 (1-3)	2 (1-3)	0.871
	30-day mortality n (%)	14 (13.2%)	56 (10.4%)	0.390

COPD: chronic obstructive pulmonary disease, PPI: proton pump inhibitor, BUN: Blood Urea Nitrogen

living in the general population and those residing in nursing homes, it ranges between 7% and 18% [11].

Patients with asymptomatic hyponatremia are more likely to fall due to gait disorders and to develop fall-associated fractures [12]. Furthermore, hyponatremia per se may be responsible for fracture [13]. Hyponatremia stimulates osteoclast activation, thereby increasing the incidence of fragility fractures by contributing to low bone mineral density and osteoporosis [14]. In our study, osteoporosis was more common in the hyponatremia group. Osteoporosis is one of the most notable risk factors for osteoporosis fragility fractures. A study examining the relationship between hyponatremia and fractures in a cohort of elderly men enrolled by the Osteoporotic Fractures in Men Study (MrOS) demonstrated that hyponatremia was associated with approximately two-fold increase in the risk of hip and morphometric vertebra fracture [15]. Similarly, another cross-sectional study showed that a serum sodium level <132 mmol/L increases the risk of osteoporotic fractures (OR = 1.46;95% CI: 1.05 to 2.04) [16].

Elderly people are more prone to hyponatremia owing to comorbidities and polypharmacy-related factors [16, 17].

Moreover, chronic hyponatremia may be associated with weakness, cognitive failure, balance disorders, falls, infections, fractures, and frailty [9, 10, 17]. Thus, it is important to determine the causes of hyponatremia in the elderly. Hyponatremia in the elderly is frequently multifactorial, with drugs and inappropriate ADH syndrome being the most common causes [18, 19]. Inappropriate ADH syndrome is typically asymptomatic and idiopathic in the elderly [20]. Moreover, many drug groups such as thiazide diuretics, Renin-Angiotensin-Aldosterone system inhibitors, antidepressants, PPIs, and antipsychotics may cause inappropriate ADH syndrome and hyponatremia in this age group [19, 20]. Several studies have shown that loop diuretics are linked to osteoporosis and fracture risk [5, 16]. Diuretics eliminate sodium and calcium either indirectly via renal excretion or directly via bone resorption from hyponatremia [14, 21]. Our findings also support that diuretic (thiazide/loop diuretic) use was more common in patients with hyponatremia. Recently, there has been an increasing number of reports of polypharmacy-related hyponatremia in the geriatric population [17]. Hyponatremia induced by prescriptions combining thiazide diuretics and NSAIDs has recently been described as a “silent epidemic” [22]. There occurs an aging-related increase in the rate of using non-steroidal anti-inflammatory drugs, antiaggregants, and anticoagulants; gastrointestinal complaints also become more prevalent with aging. Therefore, PPIs are widely prescribed and used for long time periods, without considering their harm/benefit ratio in the elderly [23]. The prevalence of PPI use increases with advanced age, especially in our country. More than half of our patients were using PPI. Conflicting results have been reported in the literature regarding the relationship between the risk of hip fracture and PPI use [24]. In a large case-control study reported from the United Kingdom, a logistic regression analysis revealed that PPI use for more than 1 year increases the risk of hip fractures by a factor of 1.44 (95% CI 1.30–1.59) [24].

The relationship between hyponatremia and antidepressant use has been mentioned in many population-based studies. Such a relationship has been most commonly shown with SSRIs [25]. We did not find any difference in SSRI-use between the groups with low and normal sodium levels. This may be secondary to underlying comorbidities and polypharmacy.

Literature studies have shown that hyponatremia increases the duration of hospital stay and the time to surgery among geriatric patients with hip fractures [6]. However, we did not detect any difference between the two groups in this regard. This may have resulted from the fact that the majority of our hyponatremic patients had mild hyponatremia.

#### Limitations

Our study had some limitations. Firstly, our study was a single-center study and its results cannot be generalized to all centers. Secondly, its retrospective design may have influenced study findings owing to missing and inaccurate data. Other factors that potentially cause fragility may have not been properly addressed. Similarly, neither patients' volume status nor gait and ataxic disorders, which may cause falls, were adequately studied.

Another limitation is the lack of repeated sodium level determinations during a hospital stay.

#### Conclusion

We demonstrated a considerably high prevalence of hyponatremia in geriatric hip fracture cases. We think that mild chronic hyponatremia is one of the most important risk factors for fragility hip fractures. We showed that the majority of hyponatremia cases are a result of polypharmacy and comorbidities. It needs to be kept in mind that medications and drug interactions may create problems with regard to hyponatremia and fragility fractures; therefore, we are of the opinion that unnecessary drug use should be avoided in this population. We also observed that even though sodium levels were low, hyponatremia did not alter the clinical course of the patients. This may have resulted from the fact that the majority of our patients had mild hyponatremia.

#### Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

#### Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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#### Conflict of interest

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